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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,526	SNODGRASS, H. RALPH	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 32-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 8 February 2005 in response to the Non-Final Office Action mailed 9 August 2004. Claims 7-9 and 32-41 were withdrawn from consideration and claims 1-6 and 10-31 were considered in the 8 February Office Action. Claim 19 was amended in the 9 August Paper. Claims 1-41 are pending and claims 1-6 and 10-31 are presently under consideration.

Response to Amendments and Arguments

Claim Objections

Objection to claim 19 as containing informalities is **withdrawn** in view of the amendment.

Claim Rejections - 35 USC § 101

Claims 19 and 20 stand rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

As stated in the previous Office Action, the claimed library is neither a machine, manufacture nor compositions of matter. It is in fact information, which is not patentable subject matter.

In response to the rejection of record, Applicant has amended claim 19 to recite that the library is stored on a computer readable media and urges withdrawal of the rejection. However, non-functional descriptive material, such as compilations of facts or data, do not become

statutory subject matter merely because they are stored on a computer readable medium. MPEP 2106 states:

> Where certain types of descriptive material, such as music, literature, art, photographs and mere arrangements or compilations of facts or data, are merely stored so as to be read or outputted by a computer without creating any functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer, then such descriptive material alone does not impart functionality either to the data as so structured, or to the computer. Such "descriptive material" is not a process, machine, manufacture or composition of matter. (Data consists of facts, which become information when they are seen in context and convey meaning to people. Computers process data without any understanding of what that data represents. Computer Dictionary 210 (Microsoft Press, 2d ed. 1994).)

Thus, the library of molecular profiles of claims 19 and 20 stored on a computer readable media are non-statutory subject matter and, therefore, remain rejected under 35 USC §101.

Claim Rejections - 35 USC § 112

Claims 19 and 20 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record.

In response to the *prima facie* case of record, Applicant cites *Atlantic Thermoplastics Co. Inc. v. Faytex Corp.* (CA FC) 23 USPQ2d 1481 and asserts that, because claims 19-20 are product by process claims, the products need not be defined in terms of structural characteristics. However, it is unclear how the cited case law supports this conclusion. The case is primarily concerned with the limiting nature of process terms in product claims for the purpose of infringement analysis. The case law does not appear to address the questions relevant to determining whether the disclosure provides adequate descriptive support for the claimed subject matter. It is noted, however, that the cited case law does provide, "the Supreme Court enunciated

a rule for products claimed with process limitations: Every patent for a product or composition of matter must identify it so that it can be recognized aside from the description of the process for making it" (page 1486). This "rule for products claimed with process limitations" would seem to be at odds with Applicant's assertion that a product claimed as a product by process need not be defined in terms of structural characteristics.

Applicant's arguments have been fully considered but are not deemed persuasive. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking adequate written description.

Claims 1-6 and 10-31 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

As stated in the previous Office Action, given the art recognized unpredictability of extrapolating *in vitro* toxicogenomic data to predict any given type of toxicity, the skilled artisan would clearly have to engage in undue empirical experimentation to confirm that the claimed method could be used to predict any particular type of toxicity in any particular organ system, let alone the broad scope contemplated in the application. The cited art teaches that merely establishing that the claimed method could be used to predict a single type of toxicity to a single organ system would require developing and characterizing the *in vitro* MSC system as a model for the appropriate target organs; performing toxicity studies with model test compounds at reasonable *in vitro* concentrations and exposure times; employing a battery of cytotoxic assays to evaluate the compounds; after evaluation of the model compounds, measuring the toxicity of unknown or previously untested agents; comparing and contrasting their toxicity with the model

compounds; and examining mechanisms of toxicity with more detailed and in-depth investigations. The art published even well after the effective filing date of the in instant application teaches that "it is too early to determine if gene expression markers for toxicity can be extrapolated from cell culture to animal systems" and "[c]learly, a great deal of additional research will be required in order to consistently link the changes seen *in vivo* and *in vitro*", and identifies developing models and tools that use gene expression measurements to ultimately predict toxicity in untested chemicals and also determine whether a similar toxic response will occur in human as a big challenge for the emerging field of toxicogenomics. Clearly, therefore, the task of developing the instant claimed method such that it can be used to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to the other known toxic compositions as asserted in the specification would require experimentation well beyond what is considered routine in the art.

In response to the *prima facie* case of record, Applicant asserts that the guidance provided in the specification with regard to culturing liver stem cells, contacting liver stem cells with a chemical composition of predetermined or unknown toxicity, detecting alterations in levels of gene or protein expression, collecting and correlating the molecular profiles, typing and ranking a test chemical composition and examples of chemicals of predetermined toxicities that may be utilized is more than adequate to allow one of ordinary skill to practice the claimed invention.

This argument has been fully considered but is not deemed persuasive. The specification teaches that the claimed methods can be used to assess toxicity of chemical compositions by comparing expression patterns of LSCs exposed to new or previously untested agents to a library

of profiles of expression induced by agents of known toxicity, such that predictions can be made as to the likely type of toxicity of the new agent (second paragraph on page 15). The specification asserts, "the outcome of such comparisons provides information for one to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to other compositions" (first paragraph on page 37). However, for the reasons set forth in detail in the previous Office Action, the skilled artisan would not be able to use the method disclosed in the application for the stated purpose without undue experimentation.

As stated in the previous Office Action, the specification is silent with regard to the predictive value of the data set presented and provides no evidence that the data can be used to establish the toxic properties of a test compound. Thus, the specification does not appear to contain a single working example of the invention such that it can be used to establish toxicity of a compound. On page 11, the specification asserts that the invention achieves the goals set forth in the specification by "exploiting the properties of pluripotent liver stem cells (LSCs)." Applicant speculates that, "[b]ecause of its pluripotency in differentiating into multiple tissue types, an isolated population of LSCs provides a much closer model to the complexity of *in vivo* systems than do traditional single cell or yeast assays" (second paragraph on page 11). However, this statement seems to be at odds with the teachings of Tugwood *et al.,* which suggest that dedifferentiation is damaging to the correlative value of an *in vitro* model system. Applicant's assertion seems to be based on a hypothesis that the relatively primitive nature of LSCs makes them more representative of the complex biology of an intact organism (see especially the discussion of the background art on pages 1-3 and the statement in the first paragraph on page

11), yet no data are presented to support this hypothesis. With regard to correlating the molecular profiles with toxicities, the specification merely teaches that repeated iteration of the method of compiling a library of molecular profiles with "a reasonably large number" of chemical compounds of similar toxicity will provide patterns of gene or protein expression, or both, associated with that toxicity. However, this simple scheme for providing correlative data fails to account for the many variables that might confound obtaining a predictive data set, such as cell type specific effects, various pathways leading to common toxic outcomes, bioconversion of some compounds to toxic metabolites and various pharmacodynamic effects present in the *in vivo* system (e.g., sequestration or compartmentalization) that would not be accounted for in the *in vitro* system. Likewise, the teachings from the specification regarding how toxicities can be typed or ranked using the claimed method provide only that the molecular profile of test composition can be compared to that of a chemical composition or library of compositions with predetermined toxicities and the outcome of the comparison provides information for one to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to the other known toxic compositions. However, these teachings are predicated on the assumption that expression profiles in LSCs are a viable model for toxicity *in vivo*, and that the system provides an accurate measure of toxicity regardless of the toxicant (i.e., to therapeutic agents, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, myotoxins, agents toxic to reproductive organs, teratogenic agents, carcinogens, agricultural chemicals, cosmetics and environmental contaminants) or organ system affected by the toxicity. Again, however, no data are provided to support this assumption. Thus, the

specification stops well short of teaching the skilled artisan how the data obtained according to the claimed method relate to the toxic properties of the test compounds.

As stated in *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003):

> It must be remembered, however, that "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure." Genentech, 108 F.3d at 1366 (quoting Brenner v. Manson, 383 U.S. 519, 536 [148 USPQ 689] (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion")). Thus, while the need for some experimentation is by no means necessarily fatal, "reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Id.

The instant claims are directed to a method of creating a molecular profile which is asserted in the application to be useful for assessing toxicity of chemical compositions by comparing expression patterns of LSCs exposed to new or previously untested agents to a library of profiles of expression induced by agents of known toxicity, such that predictions can be made as to the likely type of toxicity of the new agent. Given the extraordinarily high degree of unpredictability, which is recognized in the art, and the failure of the teachings set forth in the specification to address any of the myriad of difficulties facing one of ordinary skill in the art seeking to develop a molecular profile of chemical compositions useful for assessing toxicity, the instant disclosure amounts to no more than "general intimations of general ideas that may or may not be workable". Therefore, the disclosure fails to enable what is claimed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER